

Up to the present time, artificial-fever therapy without other therapy has been found to be unsatisfactory in the treatment of early syphilis. Certain investigative work is being conducted, combining artificial fever with drug therapy for cases of early syphilis. The value of this procedure has not been established.

We have found pyrotherapy unsatisfactory in the treatment of "Wassermann-fast" latent syphilis, and of all forms of late syphilis other than neurosyphilis.

The technical difficulties and hazards of inducing artificial fever have been eliminated to a large extent. This form of therapy should, however, be carefully controlled, and should be administered only by a thoroughly trained personnel and in an adequately equipped hospital.

The theoretical aspects of the rationale of artificial-fever therapy in syphilis have been discussed.

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### SANTIAGO RAMÓN Y CAJAL\*

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ALMOST a century ago there arose from the common people of Spain a character of such outstanding proportions and versatility as to warrant a place in history with Cervantes, Velasquez and Calderón de la Barca.

Santiago Ramón y Cajal was born at Petilla, in Aragon, on May 1, 1852. His father was a conscientious, ambitious, enterprising man who was not content to remain a "surgeon of the second class," and so, by dint of hard work and economies, he completed the course in medicine while burdened with an increasing family. From him Cajal inher-

ited his physical and mental characteristics, including a will to power, determination, ambition and a splendid memory. Cajal's mother was a woman of fine character and great beauty. It was Cajal's regret that she did not transmit her physical characteristics to any of her children.

#### BOYHOOD DAYS

Like the majority of youngsters brought up in the country, Cajal was an outdoor enthusiast who, though shy, delighted in pranks. At an early age he began to collect birds and birds' eggs. Playing at war, he developed a science of ballistics, and even wrote a small treatise on lapidary strategy.

Formal education for Cajal began at 4 years of age. By 7 or 8 he was manifesting unusual interest and appreciable talent in both drawing and painting with water colors, to the disgust and dismay of his father, who wished that nothing might interfere with the classical education he had planned for him in preparation for a medical career. Before Cajal was 8 he was profoundly impressed by the return of Spanish troops from victories in Africa; and at that early age the germ of a sense of patriotism was awakened in him. A stroke of lightning, which killed a priest while he was ringing a bell in a belfry, seriously disturbed his faith in the working of a divine providence. On the other hand, he was greatly moved by an eclipse, which had been predicted by men who could not control lightning.

Life for Cajal, when between 10 and 13 years of age, was stormy. Bored by memorizing Latin and Greek, his obstinacy and defiance led to floggings. On one occasion he was deprived of a part of his food for five months and became greatly emaciated. In order to provide his son with a trade, if not a profession, his father, in desperation, apprenticed him to a barber. Cajal made friends in this environment. By writing poetry, for the barber's assistant, to a servant girl, he obtained music lessons. For music, however, he had no talent and made little progress. When he was apprenticed at a later date to a shoemaker, he soon became so adept that he was entrusted with work of the most fastidious nature. On being permitted to return to school, he resumed drawing, at which he excelled. This led to a very embarrassing incident when he caricatured a prominent teacher, whose injured egotism would not be soothed.

#### YOUNG MANHOOD

At 16 years of age Cajal's interest in photography was awakened. He was "astonished unspeakably" by manipulations for the production of a photogenic layer on wet collodion, and "stupefied" by the development of the latent image by pyrogalllic acid. Later, he made important contributions to this art, including a work on color photography.

At 17 Cajal began the study of osteology. Bones for study were procured by father and son after dark from the local cemetery. Great was his parent's amazement and joy when his child manifested interest of high degree, a proficiency in drawing pictures of bones from all angles, and an astounding memory for anatomic details. For the ensuing

\* Address of Section Chairman. Read before the Section on Neuropsychiatry of the California Medical Association at the sixty-eighth annual session, Del Monte, May 1-4, 1939.

three years Cajal dissected in Zaragoza. During that period his attitude toward anatomy may be gleaned from his statement: "Henceforth, I saw in the cadaver, not death, with its train of gloomy suggestions, but the marvelous workmanship of it." At the end of his second year in medicine he was granted an appointment as assistant in dissection; and this enabled him to earn fees by giving lessons in practical anatomy. Subsequently, and attentively, he studied chiefly anatomy and physiology, while to the remaining subjects of the curriculum he devoted only enough effort to obtain passing grades. In June, 1873, at 21 years of age, he was granted the title *Licentiate in Medicine*.

Adhering to a plan of always having avocations, Cajal, at different times during his medical training, developed graphomania, a mania for philosophy as well as for gymnastics. Two hours of application daily to a series of exercises, some of which he improvised, served to make him a champion strong man. Of himself at that time he says: "When I walked, I showed that inelegance and rhythmic strut characteristic of the sideshow Hercules."

Caught in the military draft of Castelar, Cajal, on obtaining his medical degree, became an assistant physician in the army. In 1874 he was promoted to a captaincy and ordered to Cuba. Though he resisted the "four great vices of officialdom, tobacco, gin, gambling and women," he contracted malaria, which was followed by dysentery. After great hardship, suffering and disillusionment, he returned home at about 24 years of age.

#### TEACHING CAREER BEGINS

Showing little interest in clinical medicine, he was urged to go into teaching. During 1876 he studied anatomy and embryology, and assisted his father at the hospital. On April 28, 1877, he was made auxiliary professor on the Faculty of Medicine at Zaragoza. Further aspirations toward a teaching career obliged him to take an academic degree. At the time he took his first examination in Madrid he had never seen histologic preparations made, "nor was I capable," he said, "of carrying out the simplest microscopic examination."

At Zaragoza he managed to secure the use of the only microscope in the university, property of the department of physics. His love of microscopy was inflamed by "the amazing spectacle of the circulation of the blood." Later he purchased a microscope on the installment plan and set up a laboratory for microtechnique. He started working alone with the aid of the French versions of Henle's "General Anatomy" and Frey's "Histology and Histochemistry." He failed to pass the examinations for the chair of descriptive and general anatomy at Zaragoza, for lack of experience in speaking "before select and critical audiences" and because of "absence of pedantry." For lack of influence, he failed to obtain a similar chair at Granada. Following examination in 1879 he was appointed Director of Anatomical Museums in the Faculty of Medicine at Zaragoza, and afterward he wrote that he "owed eternal gratitude" to this appointment, which saved him from becoming a practicing physician.

While playing chess (at which he excelled), Cajal, one day in 1878, developed a pulmonary hemorrhage. His father made a diagnosis of pulmonary tuberculosis, and prescribed rest in bed, and for a time the son was very depressed. During his convalescence, he diverted himself with photography, became a manufacturer of gelatin bromide plates, and improved certain current formulas. And, against the advice of his family and friends, in 1879 he married a charming woman, whose psychology complemented his own.

#### LABORATORY INVESTIGATIONS

While director of the Anatomical Museum in Zaragoza, Cajal set up a laboratory for teaching and investigative work. His first publication was brought out in 1880. About that time he procured the leading current monographs on histology and devoted himself to studies of nervous tissue, using staining methods dependent upon silver nitrate. In 1883 he won the chair of anatomy at Valencia; and there, in 1885, he was temporarily diverted into bacteriology by the cholera epidemic. In appreciation of his work, the provincial government presented him with a Zeiss microscope. He was astonished to observe that microscopic demonstrations aroused no interest in his colleagues, who spent their time arguing and describing healthy and diseased cells without trying to see them. About that time L. Simarro, a psychiatrist and neurologist of Valencia, showed Cajal the first good preparations of nervous tissue made by Golgi's method. In 1887 Cajal himself began making Golgi preparations on a large scale.

#### NERVE TISSUE STUDIES

Appointed that year to the chair of anatomy at Barcelona, he joined a circle at a café where he met writers, politicians and men of affairs. His enthusiasm for original investigation and the intellectual renaissance of Spain increased. By 1888 Cajal was able to formulate the laws governing the morphology and connections of the nerve cells in the gray matter; and he showed that the collateral and terminal ramifications of every axis cylinder end in the gray matter by free arborizations which are applied very closely to the bodies and the dendrites of the nerve cells. Demonstration of these facts enabled him to state that the cell bodies and their processes enter into the chain of conduction, contrary to the opinion of Golgi, who felt these parts of the cells perform only a nutritive rôle. The view that the nerve impulse is transmitted by contact became inescapable since the continuity of substance between cell and cell had been excluded.

#### SILVER STAINS

Cajal then turned to the ontogenetic or embryological method, using silver stains on tissues that had not yet become myelinated. By this method cells were made to stand out complete in each section, and constant results, impossible of attainment in adult forms, became the rule. After his success with the retina and cerebellum, Cajal turned to the spinal cord, and eventually all portions of the nervous system were subjected to critical scrutiny.

Before the Anatomical Society of Germany, which met at Berlin in October, 1889, Cajal demonstrated his preparations. They were viewed with skepticism, until Kölliker became so impressed as to turn the tide in his favor. At Berlin, too, he had the opportunity to make the acquaintance of the leaders of anatomical thought in Europe. On his return trip he met Krause, who had befriended him years previously by publishing several of his communications.

#### HIS CAPACITY FOR WORK

By the time he arrived home he had become impressed with the lack of equipment even in German centers of research, and had decided that "cultural superiority depends not on the educational institutions, but upon the men." Finding "the emotion of discovery so sweet and comforting, so gently caressing to vanity and pride," he began working from 9 a. m. until midnight. His outstanding contribution of 1890 was the establishment of the genetic unity of the nerve fibers and of the dendrites. He described, for the first time, the growth-cone, a concentration of protoplasm of conical form endowed with ameboid movements at the end of the axons of chicks three days old. By 1891 he had brought out the theory of dynamic polarization. "The transmission of the nervous impulse is always from the dendritic branches and the cell body to the axon or functional process."

In 1897, realizing that the cell body does not always take part in the conduction of the nerve, he enunciated the theory of axipetal polarization, a modification of dynamic polarization. This assumes that the cell body and the dendrites transmit waves of nervous excitation toward the axon and inversely that the axon or axis cylinder carries the impulses received by the body or dendrites toward the terminal arborizations of the nerve fiber.

In April, 1892, at the age of 40 years, Cajal became Professor of Normal Histology and Pathological Anatomy at Madrid. At first he frequented the tertulia, or social club, in the Café de Levante, composed of army surgeons he had known in Cuba. He soon tired of their uninteresting conversation, however, and joined that of the Café Suizo. From these associations arose his famous "Charlas De Café." Meanwhile research was continued with unabated energy.

#### ADDRESSES ABROAD

In February, 1894, Cajal was tendered an invitation to deliver the Croonian Lecture of the Royal Society of London. He was moved to admiration of the great English institutions of learning, which he felt were admirably organized for the production of men, but not for the formation of scholars. In the same year, before the International Medical Congress at Rome, he discussed the morphology of the nerve cell. In this discussion he brought out the conclusion that intellectual power depends not on the size or number of the cerebral neurones, but on the richness of their connection processes; or, in other words, on the complexity of the association pathways to short and long distances.

Cajal was greatly depressed by the Spanish-American War, and when Clark University, at its decennial celebration in 1899, invited him to give three lectures on his work he was "surprised and perplexed." Yielding to the unanimous opinion of the government, the political press and his friends, however, he accepted the invitation and crossed the ocean to the United States. Here, almost suffocated by the heat of New York and Worcester in June and July, he was moved, by the sight of men doing manual labor in the direct rays of the sun, to exclaim: "Oh, the steely fiber of the Anglo-Saxon race." Harvard University roused his sincere admiration. On this trip, he met and enjoyed the company of Adolf Meyer.

#### REWARDS AND PRIZES

The International Medical Congress, which assembled in Paris in 1900, awarded him the international or Moscow award of 6,000 francs for the most important medical or biological work published in the triennium between meetings, and thenceforth honors were showered on Cajal. The Spanish government appropriated 80,000 pesetas for an institute of scientific research, which was opened under the name, Laboratorio de Investigaciones Biológicas. As director, Cajal was offered an annual salary of 10,000 pesetas, which, in his modesty, he refused, considering it excessive.

In 1904 Cajal completed his great work in three volumes, *Histologia del Sistema Nervioso del Hombre y de los Vertebrados*, containing 1,800 pages and 887 original illustrations. In 1905 he was awarded the Helmholtz gold medal by the Royal Academy of Sciences of Berlin. In October, 1906, with Golgi he received the Nobel prize for medicine.

The discovery, in 1913, of the gold sublimate method of staining neuroglia enabled Cajal to describe fibrous and protoplasmic types in detail, as well as a third element without processes. A two-volume work on degeneration and regeneration was completed, and printed by subscriptions of the Spanish physicians of the Argentine. Cajal was saddened by the outbreak in 1914 of the World or European War; for, unable to communicate with foreign laboratories, he felt as if he were carrying on a scientific monologue. By the end of the war most of the scientists acquainted with Spanish work had passed away. At 70 he retired from administrative duties, and on October 18, 1934, he died.

In the decade after the World War, Cajal saw erected the El Instituto Cajal, which came too late for his own work, but provided adequate quarters for his disciples. Of them, the best known in America is Pio del Río Hortego, who evolved a method for staining the "third element" of neuroglia.

Cajal stands preëminent among Spanish scientists. Great in neurohistology, he became an authority on color photography, an artist of merit and a leader in the renaissance of fine arts which sprang up before the recent Spanish civil war.

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